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| 10/713,787 | 11/13/2003 | Hans Hofland | 020681-000410 | 8755 |

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| EXAMINER | |
|---|---|
| KISHORE, GOLLAMUDI S | |

| ART UNIT | PAPER NUMBER |
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| 1615 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/713,787 | HOFLAND ET AL. | |
| | Examiner | Art Unit | |
| | Gollamudi S. Kishore, Ph.D | 1615 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *1-30,51 and 52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3-26-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's election without traverse of Group II in the reply filed on 3-1-07 is acknowledged.

Since no election requirement is made, the claims included in the prosecution are 31-50.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 31-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

According to claim 31, the lipid phase contains mucoadhesive compounds. A careful review of the specification (0044) indicates that applicant contemplates the use of Carbopol, poloxamers and Carbomers, which are hydrophilic. Therefore, it is unclear as to how the hydrophilic compounds can be present in the lipid phase. One would expect a hydrophilic compound to sequester into the hydrophilic phase and not lipid phase.

Reciting terms such as 'syndromes ***including***' in a Markush format in claims 34 and 49 is improper.

### *Claim Rejections - 35 USC § 102*

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 31, 33, 34, 37, 40, 43, 45, 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Guo (4,804,539).

Guo discloses a method of ocular delivery of ophthalmic drugs for the treatment of eye conditions using cationic liposomes. The liposomes contain phosphatidylcholine, cholesterol (neutral compounds) and a cationic lipid. The liposomes further contain mucoadhesive compounds. The active agents taught are anti-viral agents, bacteriostatic agents, anti-allergic agents, anti-inflammatory agents and anti-glaucoma agents (abstract, col. 1, lines 52-65; col. 12, lines 18-29; col. 14, line 43 through col. 17, line 30; Examples particularly V-VIII and claims).

5. Claims 31 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Szulc et al (Farm. Pol., 1988).

Szulc et al disclose a method of decreasing intraocular pressure using cationic liposomes containing pilocarpine. The liposomes contain lecithin, cholesterol and stearylamine (English abstract).

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 32, 34-36, 38-39, 41-42, 44, 46-48 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guo cited above.

Guo as pointed out above, discloses a method of ocular delivery of ophthalmic

drugs for the treatment of eye conditions using cationic liposomes. The liposomes contain phosphatidylcholine, cholesterol (neutral compounds) and a cationic lipid. The liposomes further contain mucoadhesive compounds. The active agents taught are anti-viral agents, bacteriostatic agents, anti-allergic agents, anti-inflammatory agents and anti-glaucoma agents (abstract, col. 1, lines 52-65; col. 12, lines 18-29; col. 14, line 43 through col. 17, line 30; Examples particularly V-VIII and claims). Guo however, does not specifically disclose claimed anti-inflammatory agents. Guo also does not specifically teach that the inflammatory conditions are due to different eye conditions. However, in view of Guo's teachings of generic drugs and the guidance provided, it would have been obvious to one of ordinary skill in the art to encapsulate specific drugs for the various disease states claimed with a reasonable expectation of success.

8. Claims 41-42 and 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guo cited above, further in view of Touitou (5,716,638).

The teachings of Guo have been discussed above. Although Guo teaches anti-inflammatory agents, does not specifically teach the non-steroidal anti-inflammatory agent (NSAID), diclofenac. The use of diclofenac as the NSAID for the treatment of ophthalmic conditions taught by Guo would have been obvious to one of ordinary skill in the art with a reasonable expectation of success since the reference of Touitou shows the knowledge in the art of encapsulating diclofenac in vesicular systems (Examples V and XIX).

9. Claims 41-42 and 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guo cited above, further in view of Malerhofer (5,853,753) or vice versa.

The teachings of Guo have been discussed above. As pointed out above, Guo does not disclose specific disorders of the eye which cause the eye inflammation as claimed in claims 34-36 and 49-50 or that the disorders are herpes ophthalmicus or endophthalmitis as claimed in claims 38-39.

Malerhofer discloses liposomal formulations containing active agents for the treatment of eyes diseases of allergic or viral etiology including those caused by herpes virus. The formulations further contain gel-forming agents such as Carbopol (abstract; col. 3, line 11 through col. 4, line 25; col. 5, line 50 through col. 7, line 28; col. 10, line 12 through col. 11, line 5; col. 20 line 20 through col. 21, line 30, Experiment 1 on col. 27).

It would have been obvious to one of ordinary skill in the art to use the liposomes of Gao for the various disease states with a reasonable expectation of success since the reference of Malerhofer shows that liposomal formulations containing active agents are routinely used for these disease states. Alternately, to use the liposomes of Gao in Malerhofer would have been obvious to one of ordinary skill in the art since according to Guo, the amounts of drug which is delivered in drop form in the eye may be substantially higher than that allowable in free solution form, since undesired side effects related to high free drug concentrations are reduced (col. 14, lines 61-65) and since the ocular retention of the drugs is higher (Example VIII).

10. Claims 31-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schaeffer ((Invest. Ophthalmol. Vis. Sci., 1982) by itself or further in view of Malerhofer (5,853,753).

Shaeffer explores the use of liposomes to enhance intracorneal and Tran corneal penetration of both water ad lipid-soluble drugs using penicillin G and indoxole as the representative drugs. According to Shaeffer, positively charged unilamellar liposomes enhanced transcorneal flux of penicillin G across isolated rabbit cornea more than four fold (abstract; Tables and discussion). It would have been obvious to one of ordinary skill in the art to use cationic liposomes for the delivery of water-soluble and lipid soluble drugs to treat ophthalmic diseases since Shaeffer shows that cationic liposomes are efficient in delivering drugs transcorneally. Although Shaeffer does not teach the encapsulation of claimed drugs and the treatment of specific diseases, it would have been obvious to one of ordinary skill in the art to choose appropriate drug to treat specific diseases with reasonable expectation of success since Schaeffer's studies show that both water and lipid soluble drugs can be used with the cationic liposomes. One of ordinary skill in the art would be motivated further to use the cationic liposomes of Shaeffer since the reference of Malerhofer shows that liposomal formulations containing active agents are routinely used for these disease states. Alternately, to use the liposomes of Shaeffer in Malerhofer would have been obvious to one of ordinary skill in the art since cationic liposomes are more efficient in delivering drugs ophthalmically as shown by Shaeffer.

11. Claims 41-42 and 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schaeffer ((Ophthalmol. Vis. Sci., 1982) by itself or further in view of Malerhofer (5,853,753) as set forth above, further in view of Touitou (5,716,638) cited above.

The teachings of Shaeffer and Malerhofer have been discussed above. These references do not teach the encapsulation of the anti-inflammatory drug diclofenac. The use of diclofenac as the NSAID in the cationic liposomes taught by Schaeffer for the treatment of ophthalmic conditions taught by Malerhofer would have been obvious to one of ordinary skill in the art with a reasonable expectation of success since the reference of Touitou shows the knowledge in the art of encapsulating diclofenac in vesicular systems (Examples V and XIX).

The references of Davies (pharmaceutical Research, 1992) and Durrani (international Journal of Pharmaceutics, 1992) are cited of interest.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Golamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK